

REMARKS

Applicants' representative thanks Examiner Sznaidman for the helpful telephonic interview on April 6th and for the withdrawal of rejections under 35 U.S.C. § 112, 1st and 2nd paragraph in the Advisory Action of March 29, 2010. Arguments and a second Declaration under 37 C.F.R. § 1.132 of Akihiro Tada (hereafter, 2nd Tada Declaration) are submitted herewith to address the remaining rejection under 35 U.S.C. § 103(a).

Rejection under 35 U.S.C. § 103(a)

Claims 7, 9, and 12-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ishida, et al. (EP 1147764).

As a result of the interview of April 6th, summarized herein, the Examiner stated that data showing a different effect on a different patient population or data showing a different or additional or synergistic effect on the same patient population (from Nobiletin) would be effective to overcome the rejection.

The following arguments are presented to show that the claimed compound (centaureidin) has a different result on the same patient population as Nobiletin. The 2nd Tada Declaration shows a different mechanism between Centaureidin and Nobiletin to support the arguments.

Melanin granules are produced by melanocytes in the basal epidermal layer. The melanin granules produced by the melanocyte are transferred to keratinocytes by elongation of melanocyte dendrites.

Nobiletin has an action of inhibiting production of melanin granules by inhibiting tyrosinase. However, as indicated in the 1st Tada Declaration submitted with the response of April 22, 2009, Nobiletin does not inhibit elongation of the dendrite.

Consequently, Nobiletin does not inhibit the transfer of melanin granules to keratinocytes when tyrosinase in melanocytes has been activated by exposure to UV and the like, or when tyrosinase in melanocytes is activated congenitally. Thus, Nobiletin does not sufficiently inhibit pigmented spots or dark complexion.

On the other hand, Centaureidin inhibits elongation of dendrites of melanocytes. Therefore, Centaureidin inhibits the transfer of melanin granules to keratinocytes when tyrosinase in melanocytes has been activated by exposure to UV or the like, or when tyrosinase in

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melanocytes is activated congenitally. Thus, Centaureidin effectively inhibits pigmented spot and dark complexion.

Centaureidin does not inhibit melanin production as shown in the 2nd Tada Declaration submitted herewith.

Furthermore, the effective concentration of Centaureidin required to inhibit the elongation of melanocytic dendrites is much less than the effective concentration of Nobiletin to inhibit the production of melanin granules.

Referring to the 1st Tada Declaration, submitted with the response of April 22, 2009, the Declaration shows that 10⁻⁵ % Centaureidin is effective to inhibit the elongation of melanocytic dendrites. 10⁻⁵ % of Centaureidin corresponds to about 0.27 μ M.

On the other hand, as show in the 2nd Tada Declaration attached hereto, the effective concentration of Nobiletin to inhibit the production of melanin granules is more than 1 μ M.

As discussed above, the effects of Centaureidin and Nobiletin (as taught by Ishida, et al.) are clearly different from each other. Although Centaureidin and Nobiletin are structurally similar to each other, the effectiveness observed with Centaureidin in inhibition of pigmented spot or dark complexion is not obtained using Nobiletin. This result cannot be derived from Ishida, et al. and is unexpected.

In view of Applicants' arguments and the 2nd Declaration of Akihiro Tada, withdrawal of the rejection is respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not

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reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Co-Pending Applications of Assignee

The Examiner is referred to the listings provided with the responses filed April 9, 2008 and October 20, 2009.

CONCLUSION

In view of the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: _____

June 28, 2010

By: _____

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